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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/730,632 | 12/08/2003 | Chau-Ting Yeh | 14176-003001 | 9429 |

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| EXAMINER |
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MONTANARI, DAVID A

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| ART UNIT | PAPER NUMBER |
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1632

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/730,632 | Applicant(s) YEH, CHAU-TING | |
| | Examiner David Montanari | Art Unit 1632 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 7-13 and 15-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>7/14/04</u> . | 6) <input type="checkbox"/> Other: _____ |



DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-6 and 14 in the reply filed on 7/19/2005 is acknowledged.
2. Claims 7-13, and 15-28 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **WITHOUT** traverse in Paper filed 7/19/2005.
3. Claims 1-6, and 14 are examined in the instant application.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-6, and 14 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6, and 14 of copending Application No. 10/881,758. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising a nucleotide sequence identical to SEQ ID NO: 1, wherein the presence of the said nucleic acid in a subject predisposes the subject to an abnormal liver condition comprising either non-A-E hepatitis, hepatitis B, hepatitis C or a combination thereof or colon cancer, does not reasonably provide an isolated nucleic acid comprising a nucleotide sequence having at least 70% identity to SEQ ID NO: 1, wherein the presence of the said nucleic acid in a subject predisposes the subject to any abnormal liver condition or adenocarcinoma and a cell comprising an isolated nucleic acid comprising a nucleotide sequence of at least 70% identity to SEQ ID NO: 1 wherein said cell express the nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-6, and 14 are drawn to an isolated nucleic acid comprising a nucleotide sequence at least 70% identical to SEQ ID NO:1, or a complementary sequence thereof, wherein presence of the nucleic acid in a subject predisposes the subject to an abnormal liver condition, an adenocarcinoma, or a combination thereof, wherein the abnormal liver condition is non-A-E hepatitis, hepatitis B, hepatitis C, or a combination thereof, and the adenocarcinoma is colon cancer, wherein the nucleotide sequence is at least 80%, 90%, 95%, 100% identical to SEQ ID NO: 1, and a cell comprising a nucleic acid comprising at least 70% identical to SEQ ID NO: 1.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The breadth of the claim encompasses a transgenic cell comprising a nucleotide sequence at least 70% identical to SEQ ID NO: 1, and a method of detecting any abnormal liver condition in a subject.

Whereas the nature of the invention is a diagnostic measurement for the presence of an abnormal liver condition in a subject by detecting an isolated nucleic acid and a transgenic cell expressing said isolated nucleic acid to screen for potential compounds that regulate said nucleic acid. The art teaches however, that such measurement and screening is unpredictable. The art teaches that with regard to DNA viruses, the hepatitis B virus (HBV) is the most well

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characterized. The art teaches that the HBV genome is 3.2 kb in size, with four open reading frames (ORF) that direct the synthesis of at least seven genes (Scaglioni et al., pg. 345 col. 1 lines 1-10). Scaglioni et al. continue to teach that various vectors containing the pre-genomic RNA of HBV were used to facilitate replication of HBV in hepatic carcinoma cells and in cells of a non-hepatic origin (pg. 346, col. 1 parag. 1). Scaglioni continues to teach that HBV expression is complex involving several complexes, p21, p25, p22, and p17, that are necessitate for HBV replication (pg. 345, Abstract). Hausen et al. teach that the identification of DNA tumor viruses is difficult since several of them cannot be maintained under tissue culture conditions (pg. 7820 col. 1 parag. 1 lines 1-5).

The working examples provided by the specification teach that the applicants have discovered a nucleotide sequence, SEQ ID NO: 1 that is expressed preferentially in subjects with abnormal liver conditions (pg. 1 lines 14-17). The specification further teaches that serum samples from 150 normal patients, 50 patients with chronic hepatitis B, 50 patients with chronic hepatitis C, 30 patients with biopsy-proved colon cancer, and 68 patients with chronic non-A-E hepatitis was studied for the presence of the nucleotide sequence represented by SEQ ID NO: 1 (pg. 12 lines 5-9). The specification continues to teach that identification of said nucleotide sequence was confirmed by PCR analysis using specific primers (pg. 13 lines 19-31 bridge pg. 14 lines 1-17). The specification continues that SEQ ID NO: 1 was detected in 6.7% of healthy individuals, 23.5% of patients with chronic non-A-E hepatitis, 54% of patients with chronic hepatitis B, 44% of patients with chronic hepatitis C, and 23.3% of patients with colon cancer, respectively (pg. 13 lines 30-31 bridge pg. 14 lines 1-3). The specification continues to teach that CsCl gradient analysis indicate that SEQ ID NO: 1 is a DNA virus associated with an abnormal

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liver condition, an adenocarcinoma, or a combination thereof (pg. 5, lines 16-17). However, the specification has failed to disclose any cell comprising SEQ ID NO: 1 or a protein produced by SEQ ID NO: 1. There is no disclosure of any *in vitro* data that would lead the skilled artisan to believe that SEQ ID NO: 1 codes for any protein. Further the specification fails to disclose the identification of an abnormal liver condition in subjects expressing an isolated nucleic acid sequence at least 70%, 80%, 90% or 95% identical to SEQ ID NO: 1. The specification has taught only the identification of the full-length sequence represented in SEQ ID NO: 1 in subjects suffering from chronic non-A-E hepatitis, chronic hepatitis B, chronic hepatitis C, and colon cancer. If SEQ ID NO: 1 encodes a DNA virus as the applicants assume, then the skilled artisan would require significant research to determine which parts of SEQ ID NO: 1 are required to predispose an individual to an abnormal liver condition. Only the full-length sequence of SEQ ID NO: 1 is known to be associated with an abnormal liver condition. Further it is not known in the art or disclosed in the specification whether SEQ ID NO: 1 results in an abnormal liver condition. The specification only discloses that there is a correlation with the expression of SEQ ID NO: 1 in subjects suffering from an abnormal liver condition. Further, serum was collected and analyzed from subjects. The specification provides no guidance as to what cell, if any, harbors SEQ ID NO: 1. The specification fails to disclose the claimed cell of the invention comprising SEQ ID NO: 1 in an *in vivo* or *in vivo* embodiment. The art teaches that DNA virus biology is complex and cannot be applied to *in vitro* study in all cases, further complicating and necessitating further research on the protein, if one is indeed encoded by SEQ ID NO: 1. The applicant has discovered an apparently unique nucleotide sequence that is expressed when abnormal liver function is present in a subject. Said sequence can be evaluated

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by serum analysis and does not require isolation of cells or tissue, and is merely a diagnostic measurement to evaluate predisposition to an abnormal liver condition. To elucidate potential compounds that reduce the expression of SEQ ID NO: 1 would require significant experimentation by the skilled artisan, since no disclosure of the protein encoded by SEQ ID NO: 1, other than a predicted amino acid sequence is taught.

Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the claimed invention is not enabled for its full breadth and limiting the scope of the claimed invention to an isolated nucleic acid comprising a nucleotide sequence identical to SEQ ID NO: 1, wherein the presence of the said nucleic acid in a subject predisposes the subject to an abnormal liver condition comprising either non-A-E hepatitis, hepatitis B, hepatitis C or a combination thereof or colon cancer is proper.

Claims 1-6, and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1-6, and 14 are drawn to an isolated nucleic acid comprising a nucleotide sequence at least 70% identical to SEQ ID NO:1, or a complementary sequence thereof, wherein presence of the nucleic acid in a subject predisposes the subject to an abnormal liver condition, an adenocarcinoma, or a combination thereof, wherein the abnormal liver condition is non-A-E hepatitis, hepatitis B, hepatitis C, or a combination thereof, and the adenocarcinoma is colon

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cancer, wherein the nucleotide sequence is at least 80%, 90%, 95%, 100% identical to SEQ ID NO: 1, and a cell comprising a nucleic acid comprising at least 70% identical to SEQ ID NO: 1.

When the claims are analyzed in light of the specification, the instant invention encompasses any nucleic acid comprising a nucleotide sequence that is at least 70% identical to SEQ ID NO: 1, termed "NV-F" by the applicant. However, the specification teaches only the full-length nucleotide sequence of NV-F. The specification discloses that NV-F sequence is novel and detected with high probability in subject with abnormal liver disorders. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the isolated nucleic acid sequence represented by SEQ ID NO: 1 is the only species whose complete structure is disclosed. The specification does not provide any disclosure as to what the complete structure would be of any nucleotide sequence having 70%, 80% 90% or 95% identity with SEQ ID NO:1 that would predispose a subject to an abnormal liver condition. The specification teaches no structural analysis SEQ ID NO: 1 other than nucleotide sequence and the amino acid sequence encoded by SEQ ID NO: 1. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only characteristic described, is that SEQ ID NO: 1 predisposes a subject to abnormal liver conditions. The specification does not teach any other identifying characteristic or any other related sequences that would guide the artisan to contemplate other nucleotide sequences that would predispose a subject to an abnormal liver condition.

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Applicants' attention is directed to the decision in *In re Shokal*, 113, USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim, *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97, F.2d 623, 38 USPQ 189; *In re Wahlforss et al.*, 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such a number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as halogens, consisting of four species, a reduction in practice of three, or perhaps even two, might server to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that applicant is in possession of a nucleotide sequence having at least 70%, 80%, 90%, or 95% identical to SEQ ID NO: 1. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108.

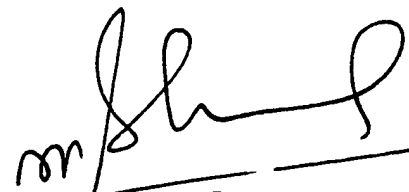
The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 1-571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 1-571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Montanari, Ph.D



RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER